

CLAIMS:

1. A method for detecting a cancer cell in a sample comprising the steps of:
 - (a) providing said sample; and
 - (b) identifying MICA or MICB expression in said sample.
- 5 2. The method of claim 2, wherein said identifying comprises binding of MICA or MICB by a MICA- or MICB-binding agent.
3. The method of claim 2, wherein said MICA- or MICB-binding agent is a first antibody.
4. The method of claim 2, wherein said first antibody is a bispecific antibody recognizing both MICA and MICB.
- 10 5. The method of claim 3, wherein said first antibody is labeled.
6. The method of claim 5, wherein said label is a radiolabel, a fluorescent label, a chemilluminous label, an enzyme, or a ligand.
7. The method of claim 3, wherein said first antibody is unlabeled and said first antibody is detected by binding of a detection agent to said first antibody.
- 15 8. The method of claim 7, wherein said detection agent is a second antibody.
9. The method of claim 8, wherein said second antibody binds to an Fc-region of said first antibody.
10. The method of claim 9, wherein said second antibody is labeled.
11. The method of claim 9, wherein said label is a radiolabel, a fluorescent label, a chemilluminous label, an enzyme, or a ligand.
- 20 12. The method of claim 3, wherein binding of said first antibody is competitive with a second antibody.
13. The method of claim 1, wherein MICA expression is identified.
14. The method of claim 1, wherein MICB expression is identified.
- 25 15. The method of claim 1, wherein MICA and MICB expression are identified.
16. The method of claim 1, wherein said identifying comprises amplifying a MICA or MICB transcript.
17. The method of claim 16, wherein said amplifying comprises PCR.
18. The method of claim 17, wherein said amplifying further comprises, prior to said PCR, reverse transcription.
- 30 19. The method of claim 17, wherein the PCR product is detected following electrophoretic separation.

20. The method of claim 17, wherein the PCR product is detected following hybridization.

21. The method of claim 17, wherein the PCR is quantitative PCR.

22. The method of claim 1, wherein the sample is selected from the group consisting of lung tissue, skin tissue, muscle tissue, liver tissue, renal tissue, colon tissue, prostate tissue, breast tissue, brain tissue, cervical tissue, pancreatic tissue, stomach tissue, testicular tissue, ovarian tissue or marrow tissue.

5 23. The method of claim 1, wherein the sample is selected from the group consisting of sputum, blood, semen, plasma, serum, lymphatic fluid, urine and stool.

24. The method of claim 1, wherein the cancer is selected from the group consisting of brain 10 cancer, lymphatic cancer, liver cancer, stomach cancer, testicular cancer, cervical cancer, leukemia, melanoma, head & neck cancer, esophageal cancer, colon cancer, breast cancer, lung cancer, ovarian cancer, prostate cancer and renal cancer.

25. The method of claim 24, wherein the cancer is colon cancer, breast cancer, lung cancer, ovarian cancer, prostate cancer or renal cancer.

15 26. A method for purifying V δ 1 $\gamma\delta$ T cells comprising the steps of:

- (a) providing a MICA or MICB polypeptide fixed to a support;
- (b) contacting said polypeptide with a starting cell population; and
- (c) separating said support from said starting cell population to produce a purified V δ 1 $\gamma\delta$ T cells population.

20 27. The method of claim 26, further comprising washing said support following step (c).

28. The method of claim 26, wherein said MICA polypeptide is fixed to said support.

29. The method of claim 26, wherein said MICB polypeptide is fixed to said support.

30. The method of claim 26, wherein said MICA and MICB polypeptides are fixed to said support.

25 31. The method of claim 26, wherein said support is a culture dish.

32. The method of claim 26, wherein said support is a dipstick.

33. The method of claim 26, wherein said support is a test tube.

34. The method of claim 26, wherein said support is a column matrix.

35. The method of claim 26, wherein said support is a bead.

30 36. The method of claim 26, wherein said support is a filter membrane.

37. The method of claim 26, wherein said starting cell population comprises peripheral blood cells.

38. The method of claim 26, wherein said starting cell population comprises lymph cells.

39. The method of claim 26, wherein said starting cell population comprises purified T-cells.

40. The method of claim 35, wherein said separating comprises centrifugation.

41. The method of claim 26, wherein the purified V δ 1 $\gamma\delta$ T cell population comprises at least about 75% V δ 1 $\gamma\delta$ T cells.

5 42. The method of claim 26, wherein the purified V δ 1 $\gamma\delta$ T cell population comprises at least about 90% V δ 1 $\gamma\delta$ T cells.

43. The method of claim 26, wherein the purified V δ 1 $\gamma\delta$ T cell population comprises at least about 95% V δ 1 $\gamma\delta$ T cells.

10 44. The method of claim 26, wherein the purified V δ 1 $\gamma\delta$ T cell population comprises at least about 99% V δ 1 $\gamma\delta$ T cells.

45. The method of claim 26, wherein the purified V δ 1 $\gamma\delta$ T cell population comprises at least about 99.9% V δ 1 $\gamma\delta$ T cells.

46. A method for enriching a cell population for V δ 1 $\gamma\delta$ T cells comprising the steps of:

15 (a) providing a MICA or MICB polypeptide linked to a fluorescent or chemiluminescent label;

(b) contacting said polypeptide with said cell population; and

(c) separating cells exhibiting fluorescence or chemiluminescence.

47. The method of claim 46, wherein said label is selected from the group consisting of fluorescein, rhodamine, green fluorescent protein and luciferase.

20 48. The method of claim 46, wherein said separating comprises cell sorting.

49. The method of claim 46, wherein said polypeptide is linked directly to said label.

50. The method of claim 46, wherein said polypeptide is linked to said label by a linking moiety.

25 51. The method of claim 50, wherein said linking moiety is a bead.

52. The method of claim 46, wherein the resulting cell population comprises at least about 99% V δ 1 $\gamma\delta$ T cells.

53. A method of targeting a therapeutic agent to a tumor cell expressing MICA or MICB on its surface comprising the steps of:

30 (a) providing a therapeutic agent having a MICA- or MICB-binding agent conjugated thereto; and

(b) contacting said therapeutic agent with said tumor cell.

54. The method of claim 53, wherein said MICA- or MICB-binding agent is an antibody.

55. The method of claim 54, wherein said antibody is humanized murine monoclonal antibody.

56. The method of claim 53, wherein said therapeutic agent is selected from the group consisting of a toxin, a cytokine, a nucleic acid encoding an antitumor agent, a chemotherapeutic and a radionuclide.

57. The method of claim 53, wherein said binding agent binds to MICA.

58. The method of claim 53, wherein said binding agent binds to MICB.

59. The method of claim 53, wherein said binding agent binds to both MICA and MICB.

10 60. The method of claim 59, wherein said binding agent is a bispecific antibody.

61. A method for treating cancer comprising the step of administering to a subject a therapeutic agent having a MICA- or MICB-binding agent conjugated thereto.

62. The method of claim 61, wherein said MICA- or MICB-binding agent is an antibody.

63. The method of claim 62, wherein said antibody is humanized murine monoclonal antibody.

15 64. The method of claim 61, wherein said therapeutic agent is selected from the group consisting of a toxin, a cytokine, a nucleic acid encoding an antitumor agent, a chemotherapeutic and a radionuclide.

65. The method of claim 61, wherein said binding agent binds to MICA.

20 66. The method of claim 61, wherein said binding agent binds to MICB.

67. The method of claim 61, wherein said binding agent binds to both MICA and MICB.

68. The method of claim 67, wherein said binding agent is a bispecific antibody.

69. The method of claim 61, wherein said cancer is selected from the group consisting of brain cancer, lymphatic cancer, liver cancer, stomach cancer, testicular cancer, cervical

25 cancer, leukemia, melanoma, head & neck cancer, esophageal cancer, colon cancer, breast cancer, lung cancer, ovarian cancer, prostate cancer and renal cancer.

70. The method of claim 61, wherein said administering comprises injection.

71. The method of claim 70, wherein said injection is intratumoral.

72. The method of claim 71, wherein said injection is intravenous.

30 74. A method for expanding V δ 1 $\gamma\delta$ T cells in a T-cell population comprising the steps of:
(a) contacting said T-cell population with MICA or MICB; and

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(b) incubating said T-cell population under conditions permitting the growth and division of T-cells.

74. The method of claim 74, wherein said contacting comprises culturing said T cell population is cultured with cells expressing MICA and MICB.

57. The method of claim 74, wherein said MICA or MICB are purified proteins.

76. The method of claim 74, wherein said starting cell population is selected from the group consisting of peripheral blood cells, lymph cells and purified T-cells.

77. A method of adoptive immunotherapy comprising the step of administering to a patient a population of purified V δ 1 γ δ T cells.

10 78. The method of claim 78, wherein said patient suffers from cancer.

79. A method of increasing expression of MICA in a cell comprising providing to said cell an expression construct comprising a coding region for MICA, wherein said coding region is under the control of a promoter active in eukaryotic cells.

80. 81. The method of claim 80, wherein said expression construct is a viral expression vector.

15 82. 81. The method of claim 80, wherein said expression construct further comprises a polyadenylation signal.

83. 82. The method of claim 80, wherein said cell is a human cell.

84. 83. The method of claim 83, wherein said human cell is in a human subject.

85. 84. The method of claim 84, wherein said human cell is a tumor cell.

20 86. 85. The method of claim 84, further comprising administering to said human subject a therapeutic agent having a MICA- or MICB-binding agent attached thereto.

87. 86. The method of claim 86, wherein said binding agent is an antibody.

88. 87. A method of increasing expression of MICB in a cell comprising providing to said cell an expression construct comprising a coding region for MICB, wherein said coding region is under the control of a promoter active in eukaryotic cells.

25 88. 89. The method of claim 88, wherein said expression construct is a viral expression vector.

90. 89. The method of claim 88, wherein said expression construct further comprises a polyadenylation signal.

91. 90. The method of claim 88, wherein said cell is a human cell.

30 92. 91. The method of claim 91, wherein said human cell is in a human subject.

93. 92. The method of claim 92, wherein said human cell is a tumor cell.

94. 93. A transgenic non-human mammal expressing a human MICA polypeptide.

95. ⁹⁴ The transgenic mammal of claim 94, wherein said mammal is a mouse.

96. ⁹⁵ The transgenic mammal of claim 95, wherein said mouse expresses human MICA in a tissue specific fashion.

97. ⁹⁶ The transgenic mammal of claim 95, wherein said mouse selectively expresses MICA in 5 intestinal epithelium.

98. ⁹⁷ A transgenic non-human mammal expressing a human MICB polypeptide.

99. ⁹⁸ The transgenic mammal of claim 98, wherein said mammal is a mouse.

100. ⁹⁹ The transgenic mammal of claim 99, wherein said mouse expresses human MICB in a tissue specific fashion.

10 102. ¹⁰⁰ The transgenic mammal of claim 100, wherein said mouse selectively expresses MICB in intestinal epithelium.

103. ¹⁰¹ A transgenic non-human mammal expressing human MICA and MICB polypeptides.

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